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13

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 07-01)

Office Action Summary	Application No.	Applicant(s)	
	09/397,957	DUONG ET AL.	
	Examiner	Art Unit	
	Frank W Lu	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☒ Responsive to communication(s) filed on *23 January 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *11-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☒ Other: *See Continuation Sheet* .

DETAILED ACTION

CONTINUED EXAMINATION UNDER 37 CFR 1.114 AFTER FINAL REJECTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 23, 2002 has been entered as Paper No:11. The claims pending in this application are claims 11-27. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn. The following rejections are based on amendment.

Sequence Rules Compliance

2. The sequencing listing filed on January 23, 2002 still fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Direct the reply to the undersigned.

Claim Rejections - 35 U.S.C. § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 16 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "higher harmonic analysis " in claim 16 is a relative term which renders the claim indefinite. The term "higher harmonic analysis" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Response to Arguments

In page 6, second paragraph of applicant's remarks, applicant argued that "[T]hose skilled in the art and the specification define ' higher harmonics' as frequencies that are the multiples of the fundamental frequency"(see specification, page 94) since "[T]he term 'higher harmonics' is a phrase well known in the field of electrochemistry and physics".

The argument has been fully considered but it is not persuasive toward the withdrawal of the rejection. As shown in page 94 of the specification, the higher harmonics is only one of examples of the multiples of the fundamental frequency. The term "the multiples of the fundamental frequency " is much broader than the higher harmonics and is not equal to the higher harmonics. Since it is unclear how high of a harmonic signal means a higher harmonic signal and how low of a harmonic signal means a lower harmonic signal, those skilled in the art will have no way to know range of higher harmonic signal. Since the specification shows that the higher harmonic frequencies can range from second to tenth harmonics or greater (page 94), there is no strandard for the higher harmonic signal.

Claim Rejections - 35 U.S.C. § 102/103

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

1.7. Claims 11 and 13 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Megerle (US Patent No. 5,874,046, filed on October 30, 1996) in light of Meade (US Patent No. 6,013,459, filed on June 12, 1997).

Megerle teaches biological warfare agent sensor system employing ruthenium-terminated oligonucleotides complementary to target live agent DNA sequences. As shown in Figure 4, the sensor cell 12 contained a single electrode or a plurality of electrodes, depending on the specificity of identification required. In the event that the sensor system was used to identify a variety of target microorganisms, each of the synthesized modified oligonucleotides with the covalent attachment of electron donor and acceptor moieties was affixed to a separate electrode such that the sensor system contained an array of electrodes, such as the linear array 68 of oligonucleotides/electrodes. All of the electrodes in an array could be contained within the same electrolyte chamber if electrochemical means such as cyclic voltammetry, pulse polarography, and impedance measurements (see columns 6 and 14) were employed to measure the electron conductance. In the presence of the targeted microorganism, hybridization occurred between the modified oligonucleic acid and the microorganism's DNA, such that the electron conductance between the electron transfer moieties greatly increased, thereby providing a means of detecting the presence of the target live microorganism (see abstract and third and fourth paragraphs in column 9). Note that, although Megerle did not directly show the steps (b) to (d) as recited in claims 11 and 13, in the absence of convincing evidence to the contrary the claimed invention, these limitations were considered as inherent to Megerle since it was known that the measurement of cyclic voltammetry included electronic input and output signals (see Meade, US Patent No. 6,013,459, filed on June 12, 1997, columns 22-24).

Therefore, Megerle teaches the limitations recited by claims 11 and 13.

Response to Arguments

In page 6, last paragraph bridging to page 8, third paragraph of applicant's remarks, applicant argued that: (1) " [A]s a preliminary matter, Applicants direct the examiner to an error in citation of Meade, which is referenced in Megerle."; and (2) Megerle " do not teach processing of detected electronic output signals".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, there was no error in citation of Meade. Meade's patent was used to support inherence rejection since Megerle did not directly show the steps (b) to (d) as recited in claims 11 and 13. However, these imitations were considered as inherent to the reference taught by Megerle in light of the teachings of Meade that related the measurement of cyclic voltammetry. Second, Megerle did teach processing of detected electronic output signals because the detection and analysis (processing) of output signals were two closely related processes and the measurement of the electrical conductance using cyclic voltammetry included the detection and analysis (processing) of output signals (for example, see Megerle, column 6 and Meade, column 24, lines 51-56). It would be impossible to image that one having ordinary skill in the art detected output signals without analyzing them.

8. Claims 12, 19, 21, and 23-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Megerle (1996) as applied to claims 11 and 13 above, and further in view of Meade (US Patent No. 6,013,459, filed on June 12, 1997) and Giancoli (Physics, principles with

applications, third edition, 1991, published by Prentice Hall, Englewood Cliffs, New Jersey 07632).

The teachings of Megerle have been summarized previously, *supra*.

Megerle does not disclose: (1) the limitation recited by claims 19, 21, and 23; (2) the detection of nucleic acid using different electronic detection methods wherein an input signal comprises an alternating current component as recited in claim 24 or comprises an AC component and a DC component as described in claim 25; and (3) a method of detecting target analytes in a sample comprising processing an electronic output signal to increase the signal to noise ratio as recited in claim 12 or comprising an input signal with a plurality of input signals as recited in claim 26 or comprising an input signal comprises the sum of multiple frequencies at a plurality of amplitudes as recited in claim 27.

Meade does teach the limitations of in claims 19, 21, and 23-26 and the limitations in step (d) of claims 12 and 27 which were not taught by Megerle. He showed that electronic detection could be carried out by different methods including time or frequency dependent methods based on AD or DC current or AC voltammetry (see column 20). Note that: (1) for the teaching in processing an electronic output signal to increase the signal to noise ratio as recited in claim 12, see column 21, third paragraph; (2) for the detection of nucleic acid using different electronic detection methods wherein an input signal comprises an alternating current component as recited in claim 24 or comprises an AC component and a DC component as described in claim 25, see columns 20-24; (3) for an input signal with a plurality of input signals as described in claim 26 and an input signal comprises the sum of multiple frequencies at a plurality of amplitudes as

recited in claim 27, see columns 20 and 22-24; and (4) although Meade did not directly show that the use of a peak recognition scheme as recited in claim 19, or signal average as recited in claim 21, or peak recognition as recited in claim 23, in the absence of convincing evidence to the contrary the claimed invention, these limitations are considered as inherent to the reference taught by Meade since these claim limitations are inherent properties of AC or DC (see Physics, principles with applications, third edition, edited by Douglas C. Giancoli, 1991, published by Prentice Hall, Englewood Cliffs, New Jersey 07632).

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have used different electronic detection methods to detect nucleic acid hybridization in view of prior art of Megerle, Meade and Giancoli because: (1) electronic detection could be carried out by different methods including time or frequency dependent methods based on AD or DC current (see Meade's patent, column 20); and (2) the simple replacement of one electronic detection method (e.g., cyclic voltammetry) from another electronic detection method (e.g., time or frequency dependent methods based on AD or/and DC current) in the detection of nucleic acid hybridization would have been, in the absence of an unexpected result, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made. As regards the motivation to make the substitution cited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

Response to Arguments

In page 8, last paragraph bridging to page 12, third paragraph of applicant's remarks, applicant argued that: (1) a variety of techniques taught by Meade, including cyclic voltammetry and AC voltammetry " do not require processing of the detected electronic output signal"; (2) "[M]egerle in view of Meade fail to teach or suggest each and every element of claims 12, 19, 21 and 23-27" since "Megerle do not teach or suggest processing an output signal to increase the signal-to-noise ration as recited in claim 12." and Meade " fail to teach or suggest methods to process the detected out signal"; (3) "[P]rocessing methods such as peak recognition are unrelated to the definition of 'peak currents' of an AC source described in Gianocoli. Peak recognition involves, in one aspect, applying mathematical algorithms to analyze the character of an electrode's response while 'peak current' is simply a definition of the maximum current generated by an AC source."; and (4) "processing of a detected output signal are not inherent properties of an AC or DC source.".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, the examiner agreed with applicant "processing of a detected output signal are not inherent properties of an AC or DC source." . However, Meade did teach processing of a detected output signal (for example, see column 24). Second, in response to applicant's argument that the references failed to show certain features of applicant's invention, it

was noted that the features upon which applicant relies (i.e., "Peak recognition involves, in one aspect, applying mathematical algorithms to analyze the character of an electrode's response while 'peak current' is simply a definition of the maximum current generated by an AC source.") were not recited in the rejected claim(s). Although the claims were interpreted in light of the specification, limitations from the specification were not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Therefore, without defining what peak recognition in claim 23, peak recognition scheme of AC or AD could be considered as peak recognition.

9. Claims 12, 16, 21, and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Megerle (1996) in light of Meade (1997) as applied to claims 11 and 13 above, and further in view of Singhal *et al.,* (Anal. Chem. 69, 3552-3557, September 1, 1997).

The teachings of Megerle in light of Meade have been summarized previously, *supra*.

Megerle in light of Meade does not disclose a method of detecting target analytes in a sample comprising processing an electronic output signal to increase the signal to noise ratio as described in step (d) of claim 12 or the processing comprised analysis of higher harmonic signals as recited in claim 16 or signal average as recited in claim 21 or spectral analysis as recited in claim 22.

Singhal *et al.,* do teach direct electrochemical detection of purine- and pyrimidine-based nucleotides with sinusoidal voltammetry wherein analysis process included increase electronic output signal to noise ratio (see left column in page 3555), analysis of higher harmonic signals

(see Figure 2 in page 3555 and Figure 4 in page 35556), and signal averaging (see page 3554, right column, second paragraph) and spectral analysis (page 3554, left column, last paragraph).

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have detected nucleic acid hybridization using sinusoidal voltammetry wherein analysis process included increase electronic output signal to noise ratio, analysis of higher harmonic signals, and signal averaging and spectral analysis in view of prior art of Megerle in light of Meade and Singhal *et al.*, because the simple replacement of one electronic detection method (e.g., cyclic voltammetry) from another electronic detection method (e.g., sinusoidal voltammetry) in the detection of nucleic acid hybridization would have been, in the absence of an unexpected result, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made. As regards the motivation to make the substitution cited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

Response to Arguments

In page 13, third paragraph bridging to page 14, first paragraph of applicant's remarks, applicant argued that: (1) "[M]egerle in view of Singhai fail to render claims 12, 16, 21, and 22

obvious." since Megerle "fails to teach or suggest processing of an output signal" and Singhal *et al.,* fail to teach or suggest use of methods such as voltammetry and higher harmonics analysis "as applied to nucleic acid covalently bound to an electrode."; (2) "[S}inghai teach away from the limitations of claim 12 by citing the disadvantages of nucleic acids absorbed on surfaces of electrodes for flow through detection schemes."; and (3) "[T]he examiner has not pointed to where in Singhal the suggestion exists for applying higher harmonic analysis and FFT algorithms, signal averaging, or spectral analysis to output signals detected from electrodes comprising covalently attached nucleic acids".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, Megerle did teach processing of an output signal (see above Response to Arguments of the rejection under 35 U.S.C. 102 (e)/103(a)). Second, the examiner agreed with applicant that Singhal *et al.,* did not teach to apply a nucleic acid covalently bound to an electrode and use higher harmonic analysis and FFT algorithms, signal averaging, or spectral analysis to output signals detected from electrodes comprising covalently attached nucleic acids However, in response to applicant's argument that there was no suggestion to combine the references, the examiner recognized that obviousness could only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there was some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Megerle in light of Meade taught everything in claim 12 except increasing

the signal to noise ratio as described in step (d) of claim 12 and the processing comprised analysis of higher harmonic signals or signal average or spectral analysis as recited in claims 16, 21, and 22 that enclosed by Singhal *et al.*. Since knowledge that sinusoidal voltammetry could be used in analysis process included increase electronic output signal to noise ratio, analysis of higher harmonic signals, signal averaging and spectral analysis was generally available to one of ordinary skill in the art at the time the invention was made. Therefore, in the absence of an unexpected result, the simple replacement of one electronic detection method (e.g., cyclic voltammetry) from another electronic detection method (e.g., sinusoidal voltammetry) in the detection of nucleic acid hybridization would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made. Third, Singhal *et al.,* did teach that nucleic acids absorbed on surfaces of electrodes for flow through detection. However, nucleic acids absorbed on surfaces of electrodes was not a disadvantage as suggested by applicant but was another way to attach nucleic acids to surfaces of electrodes. Note that a capture binding ligand such as nucleic acid was attached to surfaces of electrodes in claim 12 of this instant application.

10. Claims 12 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Megerle (1996) in light of Meade (1997) as applied to claims 11 and 13 above, and further in view of Cheever *et al.,* (Comput. Appl. Biosci (CABIOS), 7, 143-154, 1991).

The teachings of Megerle in light of Meade have been summarized previously, *supra*.

Megerle in light of Meade does not disclose a method of detecting target analytes in a sample comprising processing an electronic output signal to increase the signal to noise ratio as described in step (d) of claim 12 and a fast Fourier transform (FFT) analysis as described in claim 17.

Cheever *et al.,* do teach a method of detecting target analytes in a sample comprising a fast Fourier transform (FFT) analysis. FFT analysis has been a well-known algorithm from the field of signal processing and could be used for the comparison of DNA sequences by correlation (see right column of page 143 and right column of page 144) and could be traded off increasing or decreasing signal to noise ratio as described in claim 12 (see abstract in page 143 and right column of page 152).

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have been detected nucleic acid hybridization using cyclic voltammetry as suggested by Megerle and analyzed detecting signals by FFT analysis wherein analysis process included increase electronic output signal to noise ratio in view of Megerle in light of Meade and Cheever *et al.*. One having ordinary skill in the art would have been motivated to modify Megerle's method and combine above methods together because FFT analysis has been a well-known algorithm from the field of signal processing (a method for standard frequency analysis, see below) and could be used in different output signal analysis (see Cheever *et al.*,right column of page 143 and right column of page 144). One having ordinary skill in the art at the time the invention was made would have

been a reasonable expectation of success to analyze the hybridization signal collected by cyclic voltammetry using FFT.

Response to Arguments

In page 14, fourth paragraph of applicant's remarks, applicant argued that "[M]egerle in view of Cheever fail to teach or suggest each and every element of claims 12 and 17." since "[M]egerle fail to teach or suggest processing of an electronic output signal to increase the signal-to-noise ratio," and Cheever *et al.,* "do not teach or suggest applying FFT to processing of an electronic output signal to increase the signal-to-noise ratio.".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection because Megerle in light of Meade did teach processing of an output signal (see above Response to Arguments of the rejection under 35 U.S.C. 102 (e)/103(a)) while Cheever *et al.,* did teach applying FFT to processing of an electronic output signal to increase the signal-to-noise ratio (see right column in page 152).

11. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Megerle (1996) in light of Meade (1997) and Cheever *et al.,* (1991) as applied to claims 11-13 and 17 above, and further in view of Wood *et al.,* (IEEE Transactions on Biomedical Engineering, 39, 730-740, 1992).

The teachings of Cheever *et al.,* and Megerle in light of Meade have been summarized previously, *supra*.

Cheever *et al.,* and Megerle in light of Meade do not disclose a method of detecting target analytes in a sample comprising joint-time frequency transformation (JTFT) analysis as described in claim 18.

Wood *et al.,* teach heart sound dynamic frequency analysis using JTFT (see abstract in page 730). Note both FFT and JTFT are standard frequency analysis techniques but may be used for different purposes (right column in page 730).

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have been detected nucleic acid hybridization using cyclic voltammetry and analyzed detecting signals by JTFT analysis in view of prior art of Cheever *et al.,* and Megerle in light of Meade and Wood *et al.,* because the simple replacement of one frequency analysis method (e.g., FFT) from another frequency analysis method (e.g., JTFT) during the process of analyzing hybridization signal would have been, in the absence of an unexpected result, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made. As regards the motivation to make the substitution cited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

Response to Arguments

In page 15, last paragraph bridging to page 16, second paragraph of applicant's remarks, applicant argued that: (1) "[M]egerle in view of Cheever further in view of Wood fail to teach or suggest each and every element of claim 18" since " "[M]egerle in view of Cheever do not disclose a method for processing an electronic output signal or processing of an electronic output signal to increase the signal-to-noise ratio." and Wood *et al.,* "fail to teach or suggest use of joint time frequency transforms to process electronic output signals." ; and (2) " [A] person of ordinary skill in electrochemistry dealing with electronic signals and electronic noise would not be reasonably expected or motivated to look to analysis of sound frequencies."

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, Megerle in light of Meade did teach processing of an output signal (see above Response to Arguments of the rejection under 35 U.S.C. 102 (e)/103(a)) while Cheever *et al.,* did teach applying FFT to processing of an electronic output signal to increase the signal-to-noise ratio (see right column in page 152). Second, the examiner agreed with applicant that Wood *et al.,* did not teach use of joint time frequency transforms to process electronic output signals. However, applicant could not show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Third, since applicant did not provide an evidence to show why " [A] person of ordinary skill in electrochemistry dealing with electronic signals and electronic noise would not be reasonably expected or motivated to look to analysis of sound frequencies.",

in the absence of an unexpected result, the simple replacement of one frequency analysis method (e.g., FFT) from another frequency analysis method (e.g., JTFT) during the process of analyzing hybridization signal would have been, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made.

12. Claim 20 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Megerle (1996) in light of Meade (1997) as applied to claims 11 and 13 above, and further in view of Nederlof *et al.,* (Cytometry 13, 846-852, 1992).

The teachings of Megerle in light of Meade have been summarized previously, *supra*.

Megerle in light of Meade does not disclose a method of detecting target analytes in a sample comprising a digital filter as described in claim 20 or spectral analysis as described in claim 22.

Nederlof *et al.,* do teach a method of detecting target analytes in a sample (quantification of fluorescence *in situ* hybridization signal by image cytometry) comprising a digital filter and spectral analysis (see abstract in page 846 and pages 849-851). Nederlof *et al.*, also teach spectral analysis since *in situ* hybridization signals were collected by epi-fluorescence microscope using different excitation filter having different wavelengths (see right column of page 847 and Table 1 in page 848).

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have detected nucleic acid hybridization using image cytometry comprising a digital filter and spectral analysis in view

of prior art of Megerle in light of Meade and Nederlof *et al.,* because the simple replacement of one electronic detection method (e.g., cyclic voltammetry) from another electronic detection method (e.g., image cytometry) in the detection of nucleic acid hybridization would have been, in the absence of an unexpected result, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made. As regards the motivation to make the substitution cited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

Response to Arguments

In page 17, second and third paragraph pf applicant's remarks, applicant argued that: (1) "[M]egerle in view of Nederlof do not satisfy the requirements for establishing a case of *prima facie* obviousness for claims 11-13." since "[M]egerle fails to teach or suggest processing an electronic output signal or processing of an electronic output signal to increase the signal-to-noise ratio." and Nederlof *et al.,* "does not teach processing of detected electronic output signals." ; and (2) "[A]pplicants were unable to identify a passage in Nederlof cited by the Examiner as reciting processing by spectral analysis.".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, Megerle in light of Meade did teach processing of an output signal (see above Response to Arguments of the rejection under 35 U.S.C. 102 (e)/103(a)). Second, the examiner agreed with applicant that Megerle did not teach processing of an electronic output signal to increase the signal-to-noise ratio recited in claim 12. However, the rejection was based on independent claims 11 and 13, not independent claim 12. Third, Nederlof *et al.,* did teach processing of detected electronic output signals since fluorescence images collected and analyzed by Nederlof *et al.,* was electronic output signals. Fourth, Nederlof *et al.*, did teach spectral analysis since *in situ* hybridization signals were collected by epi-fluorescence microscope using different excitation filter having different wavelengths (see right column of page 847 and Table 1 in page 848).

Conclusion

13. This is a RCE of applicant's earlier Application No. 09/397,957. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

14. No claim is allowed.

15. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank L., Ph.D., whose telephone number is (703) 305-1270. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
February 22, 2002

ETHAN C. WHISENANT
PRIMARY EXAMINER

F.D.

Re-run

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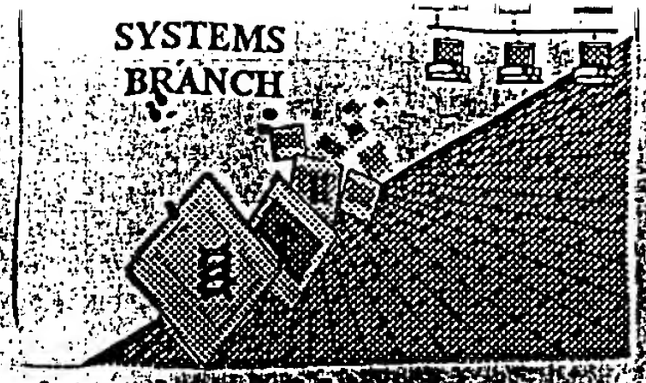

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Application Serial Number: 09/399,957A
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Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses:

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Revised 01/29/2002